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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,778	09/18/2003	Alain Goossens	2676-6085US	8721

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

NOTIFICATION DATE	DELIVERY MODE
10/12/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/666,778	**Applicant(s)** GOOSSENS ET AL.	
	Examiner Russell Kallis	**Art Unit** 1638	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 September 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: 20-21.
   Claim(s) rejected: 1-13 and 15-19.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: See Continuation Sheet.

This rejection is maintained for the reasons of record set forth in the Official action mailed 7/31/2007. Applicant's arguments filed 9/28/2007 have been considered but are not deemed persuasive.
Applicant asserts that the references do not teach the exact function of the ABC transporter AtPGP1 and thus the claim limitation is not taught in the prior art (response page 7 lines 3-7). It would be remiss upon the examiner if it was not pointed out that the claims are not drawn to any specific or exact activity or function other than the broadly claimed transport of an unspecified secondary metabolite. Further, the prior art suggests that AtPGP1 transports a regulator involved in light dependent hypocotyl elongation, and speculates that it may be a peptide. However one must also consider what is well-known in the art, that hypocotyl elongation is a response to auxin, which is a secondary metabolite. Moreover, from Applicant's specification on page 11, AtPGP1 is listed as an embodiment of the invention;

"An MDR-like gene (atpgp1) has also been identified in A. thaliana, which encodes a putative P-glycoprotein homolog. This atpgp1 gene was found to share significant sequence homology and structural organization with human MDR genes. Other MDR homologues have been found in potato and barley. Genes encoding ABC-transporters of the present invention which may be operably linked with a promoter for expression in a plant species may be derived from a chromosomal gene, cDNA, a synthetic gene, or combinations thereof.";

and thus contrary to Applicant's assertions one of ordinary skill would have a reasonable expectation of success.
Applicant points to Claims 1, 7 and 16 as reciting the limitations "selecting transformed plant cells having an induced or enhanced production or secretion of at least one secondary metabolite" and "selecting transformed plant cells exhibiting enhanced transport of said at least one secondary metabolite into a vacuole" as examples of limitations that are not met in the references cited (response page 7). Clearly, the references direct one of ordinary skill to characterize the ABC transporters for the type of secondary metabolite transported and vacuolar transport using a transgenic plant approach (see Theodoulou page 84 section 4. the emergence of plant ABC transporters in columns 1-2, especially lines 5-15 of column 2; and all of section 5 on page 86, especially column 2 lines 12-24); and thus one of ordinary skill in the art is directed to select for induced or enhanced activity.
Applicants assertion that selection was not based upon either production of the gene product of the AtPGP1 gene or its' location of transport is inconsistent with the teachings of the reference (response page 7). Sidler teaches that plants overexpressing the AtPGP1 ABC transporter grew longer hypocotyls when compared to antisense and wild type plants and this was correlated with increased expression of the AtPGP1 gene product as made evident by immunoblotting of microsomal membrane fractions (on page 1624 column 1 lines 18-31). Moreover, one of ordinary skill in the art would have appreciated that the hypocotyl elongation observed in the transgenic plants was most likely a result of increased auxin transport into the hypocotyl cells. Further, Applicant's IDS teaches the state of the prior art with reference to WO 98/21938 (Rea) that teaches GS-X an ABC transporter that is active in storing pigment (i.e. a secondary metabolite) by transport into Maize vacuoles and a teaches a method for increasing pigment transport into plant vacuoles by transformation with GS-X (see pages 1-6 and 87-89; and claim 25). Therefore, the state of the art was actively involved in isolating, characterizing i.e. selecting for expression above wild type including vacuolar accumulation, and transforming said ABC transporter genes into plants. Applicant's remarks concerning improper hindsight are not wel founded and addressed supra.
Applicant's assertion that any metabolite transported by AtPGP1 is a primary metabolite because it is involved in survival and hence is a primary metabolite is based upon Applicant's faulty interpretation of the results of antisense experiments where a complete knockout of gene expression was not observed. This reasoning is faulty because it is well known in the art that it is rare to have a complete knock out of gene expression using antisense. Further, Applicant's IDS teaches the state of the prior art with reference to WO 98/21938 (Rea) that teaches GS-X an ABC transporter that is active in storing pigment (i.e. a secondary metabolite) by transport into Maize vacuoles and a teaches a method for increasing pigment transport into plant vacuoles by transformation with GS-X (see pages 1-6 and 87-89; and claim 25). Furthermore, In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that the references do not teach the limitations discussed supra, the test for obviousness is not that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Applicant asserts that the role suggested in the art for P-gp is clearly distinct from the claim limitation of "capable of enhancing or stimulating the production or secretion of that [secondary metabolite] compound" (response page 8). However, the claims are not limited only to 'enhancing or stimulating', but rather recite inducing (claim 1). Nonetheless, the increased expression of AtPGP1 and the increase in hypocotyls elongation observed in Sidler as stated supra, combined with the knowledge of the structure of AtPGP1 as an ABC transporter, it would be well understood by one of ordinary skill that the increased expression of AtPGP1 would result in the increased transport of a secondary metabolite.
Applicant assertion that the declaration showed three genes known to be involved in the synthesis and/or compartmentation does not teach as to why anyone would expect there to be an increase in the compartmentation or transport of their respective products since none of them are responsible for compartmentation or transport whatsoever. None of those results are unexpected. The claims are drawn to transporters not biosynthetic enzymes. In fact none of the examples submitted in the Declaration of Alain Goossens are transporters or possess the Walker A and B motif as well as the nucleotide binding fold as recited in the claims other than those already disclosed in the specification in Table 2 on page 28. Applicant's conclusions on page 8 of the response, that the possibility of a gene being involved in the synthesis 'and/or' compartmentation of a secondary metabolite does not translate into a reasonable expectation of success that the gene is involved in the production or secretion of a secondary metabolite. Clearly, Applicant is comparing apples and oranges because the

claims are not drawn to only to increased synthesis, but rather are drawn to induced or enhanced production or secretion; or enhanced transport.

The refutation of Applicant's declaration is provided supra. Those portions of the declaration showing unexpected results have already been considered, they are part of the original specification and have deemed allowable; see objected claims 20-21. The declaration was not given any additional weight because it provided no new evidence for the claimed genus of ABC transporters. Applicant's statements that the Examiner has provided no evidence other than to indicate that it was considered irrelevant is a gross misrepresentation of the Examiner's remarks. Clearly an analysis was performed and the declaration was evaluated. Moreover, Applicant has failed to respond to the Examiner's arguments per in re Lindner, and is repeated below.

Applicant has demonstrated an induced or enhanced production or secretion of only a nicotine based alkaloid in tobacco transformed with SEQ ID NO: 1. In contrast, the method claims are broadly drawn to a multitude of ABC sequences from a multitude of sources having no specific secondary metabolite specificity, including animal or plant genes encoding ABC transporters; see In re Lindner, 173 USPQ 356 (CCPA 1972) and In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims.

No claim is allowed.

Claims 20-21 are objected to as being dependent upon rejected base claim 15, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
October 5, 2007

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER